```
        10          20          30          40          50
AAT TCC GGA GCC ATG GTG AAC GAA GCC AGA GGA AAC AGC AGC CTC AAC CCC
TTA AGG CCT CGG TAC CAC TTG CTT CGG TCT CCT TTG TCG TCG GAG TTG GGG
Asn Ser Gly Ala Met Val Asn Glu Ala Arg Gly Asn Ser Ser Leu Asn Pro>

       60          70          80          90         100
TGC TTG GAG GGC AGT GCC AGC AGT GGC AGT GAG AGC TCC AAA GAT AGT TCG
ACG AAC CTC CCG TCA CGG TCG TCA CCG TCA CTC TCG AGG TTT CTA TCA AGC
Cys Leu Glu Gly Ser Ala Ser Ser Gly Ser Glu Ser Ser Lys Asp Ser Ser>

      110         120         130         140         150
AGA TGT TCC ACC CCG GGC CTG GAC CCT GAG CGG CAT GAG AGA CTC CGG GAG
TCT ACA AGG TGG GGC CCG GAC CTG GGA CTC GCC GTA CTC TCT GAG GCC CTC
Arg Cys Ser Thr Pro Gly Leu Asp Pro Glu Arg His Glu Arg Leu Arg Glu>

     160         170         180         190         200
AAG ATG AGG CGG CGA TTG GAA TCT GGT GAC AAG TGG TTC TCC CTG GAA TTC
TTC TAC TCC GCC GCT AAC CTT AGA CCA CTG TTC ACC AAG AGG GAC CTT AAG
Lys Met Arg Arg Arg Leu Glu Ser Gly Asp Lys Trp Phe Ser Leu Glu Phe>

    210         220         230         240         250
TTC CCT CCT CGA ACT GCT GAG GGA GCT GTC AAT CTC ATC TCA AGG TTT GAC
AAG GGA GGA GCT TGA CGA CTC CCT CGA CAG TTA GAG TAG AGT TCC AAA CTG
Phe Pro Pro Arg Thr Ala Glu Gly Ala Val Asn Leu Ile Ser Arg Phe Asp>

   260         270         280         290         300
CGG ATG GCA GCA GGT GGC CCC CTC TAC ATA GAC GTG ACC TGG CAC CCA GCA
GCC TAC CGT CGT CCA CCG GGG GAG ATG TAT CTG CAC TGG ACC GTG GGT CGT
Arg Met Ala Ala Gly Gly Pro Leu Tyr Ile Asp Val Thr Trp His Pro Ala>

  310         320         330         340         350
GGT GAC CCT GGC TCA GAC AAG GAG ACC TCC TCC ATG ATG ATC GCC AGC ACC
CCA CTG GGA CCG AGT CTG TTC CTC TGG AGG AGG TAC TAC TAG CGG TCG TGG
Gly Asp Pro Gly Ser Asp Lys Glu Thr Ser Ser Met Met Ile Ala Ser Thr>
```

Fig. 1A

```
360          370          380          390          400
  x    x    x    x    x    x    x    x    x    x
GCC GTG AAC TAC TGT GGC CTG GAG ACC ATC CTG CAC ATG ACC TGC TGC CGT
CGG CAC TTG ATG ACA CCG GAC CTC TGG TAG GAC GTG TAC TGG ACG ACG GCA
Ala Val Asn Tyr Cys Gly Leu Glu Thr Ile Leu His Met Thr Cys Cys Arg>

410          420          430          440          450
  x    x    x    x    x    x    x    x    x    x
CAG CGC CTG GAG GAG ATC ACG GGC CAT CTG CAC AAA GCT AAG CAG CTG GGC
GTC GCG GAC CTC CTC TAG TGC CCG GTA GAC GTG TTT CGA TTC GTC GAC CCG
Gln Arg Leu Glu Glu Ile Thr Gly His Leu His Lys Ala Lys Gln Leu Gly>

460          470          480          490          500          510
  x    x    x    x    x    x    x    x    x    x    x    x
CTG AAG AAC ATC ATG GCG CTG CGG GGA GAC CCA ATA GGT GAC CAG TGG GAA
GAC TTC TTG TAG TAC CGC GAC GCC CCT CTG GGT TAT CCA CTG GTC ACC CTT
Leu Lys Asn Ile Met Ala Leu Arg Gly Asp Pro Ile Gly Asp Gln Trp Glu>

          520          530          540          550          560
     x    x    x    x    x    x    x    x    x    x
GAG GAG GAG GGA GGC TTC AAC TAC GCA GTG GAC CTG GTG AAG CAC ATC CGA
CTC CTC CTC CCT CCG AAG TTG ATG CGT CAC CTG GAC CAC TTC GTG TAG GCT
Glu Glu Glu Gly Gly Phe Asn Tyr Ala Val Asp Leu Val Lys His Ile Arg>

        570          580          590          600          610
     x    x    x    x    x    x    x    x    x    x
AGT GAG TTT GGT GAC TAC TTT GAC ATC TGT GTG GCA GGT TAC CCC AAA GGC
TCA CTC AAA CCA CTG ATG AAA CTG TAG ACA CAC CGT CCA ATG GGG TTT CCG
Ser Glu Phe Gly Asp Tyr Phe Asp Ile Cys Val Ala Gly Tyr Pro Lys Gly>

       620          630          640          650          660
  x    x    x    x    x    x    x    x    x    x
CAC CCC GAA GCA GGG AGC TTT GAG GCT GAC CTG AAG CAC TTG AAG GAG AAG
GTG GGG CTT CGT CCC TCG AAA CTC CGA CTG GAC TTC GTG AAC TTC CTC TTC
His Pro Glu Ala Gly Ser Phe Glu Ala Asp Leu Lys His Leu Lys Glu Lys>

      670          680          690          700          710
  x    x    x    x    x    x    x    x    x    x
GTG TCT GCG GGA GCC GAT TTC ATC ATC ACG CAG CTT TTC TTT GAG GCT GAC
CAC AGA CGC CCT CGG CTA AAG TAG TAG TGC GTC GAA AAG AAA CTC CGA CTG
Val Ser Ala Gly Ala Asp Phe Ile Ile Thr Gln Leu Phe Phe Glu Ala Asp>
```

Fig. 1B

```
    720          730          740          750          760
    x    x       x    x       x    x       x    x       x    x
ACA TTC TTC CGC TTT GTG AAG GCA TGC ACC GAC ATG GGC ATC ACT TGC CCC
TGT AAG AAG GCG AAA CAC TTC CGT ACG TGG CTG TAC CCG TAG TGA ACG GGG
Thr Phe Phe Arg Phe Val Lys Ala Cys Thr Asp Met Gly Ile Thr Cys Pro>

   770          780          790          800          810
    x    x       x    x       x    x       x    x       x    x
ATC GTC CCC GGG ATC TTT CCC ATC CAG GGC TAC CAC TCC CTT CGG CAG CTT
TAG CAG GGG CCC TAG AAA GGG TAG GTC CCG ATG GTG AGG GAA GCC GTC GAA
Ile Val Pro Gly Ile Phe Pro Ile Gln Gly Tyr His Ser Leu Arg Gln Leu>

   820          830          840          850          860
    x    x       x    x       x    x       x    x       x    x
GTG AAG CTG TCC AAG CTG GAG GTG CCA CAG GAG ATC AAG GAC GTG ATT GAG
CAC TTC GAC AGG TTC GAC CTC CAC GGT GTC CTC TAG TTC CTG CAC TAA CTC
Val Lys Leu Ser Lys Leu Glu Val Pro Gln Glu Ile Lys Asp Val Ile Glu>

   870          880          890          900          910
    x    x       x    x       x    x       x    x       x    x
CCA ATC AAA GAC AAC GAT GCT GCC ATC CGC AAC TAT GGC ATC GAG CTG GCC
GGT TAG TTT CTG TTG CTA CGA CGG TAG GCG TTG ATA CCG TAG CTC GAC CGG
Pro Ile Lys Asp Asn Asp Ala Ala Ile Arg Asn Tyr Gly Ile Glu Leu Ala>

   920          930          940          950          960
    x    x       x    x       x    x       x    x       x    x
GTG AGC CTG TGC CAG GAG CTT CTG GCC AGT GGC TTG GTG CCA GGC CTC CAC
CAC TCG GAC ACG GTC CTC GAA GAC CGG TCA CCG AAC CAC GGT CCG GAG GTG
Val Ser Leu Cys Gln Glu Leu Leu Ala Ser Gly Leu Val Pro Gly Leu His>

   970          980          990          1000         1010         1020
    x    x       x    x       x    x       x    x       x    x       x
TTC TAC ACC CTC AAC CGC GAG ATG GCT ACC ACA GAG GTG CTG AAG CGC CTG
AAG ATG TGG GAG TTG GCG CTC TAC CGA TGG TGT CTC CAC GAC TTC GCG GAC
Phe Tyr Thr Leu Asn Arg Glu Met Ala Thr Thr Glu Val Leu Lys Arg Leu>

         1030         1040         1050         1060         1070
    x    x       x    x       x    x       x    x       x    x
GGG ATG TGG ACT GAG GAC CCC AGG CGT CCC CTA CCC TGG GCT CTC AGT GCC
CCC TAC ACC TGA CTC CTG GGG TCC GCA GGG GAT GGG ACC CGA GAG TCA CGG
Gly Met Trp Thr Glu Asp Pro Arg Arg Pro Leu Pro Trp Ala Leu Ser Ala>
```

Fig. 1C

```
      1080       1090       1100       1110       1120
CAC CCC AAG CGC CGA GAG GAA GAT GTA CGT CCC ATC TTC TGG GCC TCC AGA
GTG GGG TTC GCG GCT CTC CTT CTA CAT GCA GGG TAG AAG ACC CGG AGG TCT
His Pro Lys Arg Arg Glu Glu Asp Val Arg Pro Ile Phe Trp Ala Ser Arg>

      1130       1140       1150       1160       1170
CCA AAG AGT TAC ATC TAC CGT ACC CAG GAG TGG GAC GAG TTC CCT AAC GGC
GGT TTC TCA ATG TAG ATG GCA TGG GTC CTC ACC CTG CTC AAG GGA TTG CCG
Pro Lys Ser Tyr Ile Tyr Arg Thr Gln Glu Trp Asp Glu Phe Pro Asn Gly>

      1180       1190       1200       1210       1220
CGC TGG GGC AAT TCC TCT TCC CCT GCC TTT GGG GAG CTG AAG GAC TAC TAC
GCG ACC CCG TTA AGG AGA AGG GGA CGG AAA CCC CTC GAC TTC CTG ATG ATG
Arg Trp Gly Asn Ser Ser Ser Pro Ala Phe Gly Glu Leu Lys Asp Tyr Tyr>

    1230       1240       1250       1260       1270
CTC TTC TAC CTG AAG AGC AAG TCC CCC AAG GAG GAG CTG CTG AAG ATG TGG
GAG AAG ATG GAC TTC TCG TTC AGG GGG TTC CTC CTC GAC GAC TTC TAC ACC
Leu Phe Tyr Leu Lys Ser Lys Ser Pro Lys Glu Glu Leu Leu Lys Met Trp>

   1280       1290       1300       1310       1320
GGG GAG GAG CTG ACC AGT GAA GCA AGT GTC TTT GAA GTC TTT GTT CTT TAC
CCC CTC CTC GAC TGG TCA CTT CGT TCA CAG AAA CTT CAG AAA CAA GAA ATG
Gly Glu Glu Leu Thr Ser Glu Ala Ser Val Phe Glu Val Phe Val Leu Tyr>

  1330       1340       1350       1360       1370
CTC TCG GGA GAA CCA AAC CGG AAT GGT CAC AAA GTG ACT TGC CTG CCC TGG
GAG AGC CCT CTT GGT TTG GCC TTA CCA GTG TTT CAC TGA ACG GAC GGG ACC
Leu Ser Gly Glu Pro Asn Arg Asn Gly His Lys Val Thr Cys Leu Pro Trp>

1380       1390       1400       1410       1420
AAC GAT GAG CCC CTG GCG GCT GAG ACC AGC CTG CTG AAG GAG GAG CTG CTG
TTG CTA CTC GGG GAC CGC CGA CTC TGG TCG GAC GAC TTC CTC CTC GAC GAC
Asn Asp Glu Pro Leu Ala Ala Glu Thr Ser Leu Leu Lys Glu Glu Leu Leu>
```

Fig. 1D

```
1430        1440        1450        1460        1470
  x     x     x     x     x     x     x     x     x     x
CGG GTG AAC CGC CAG GGC ATC CTC ACC ATC AAC TCA CAG CCC AAC ATC AAC
GCC CAC TTG GCG GTC CCG TAG GAG TGG TAG TTG AGT GTC GGG TTG TAG TTG
Arg Val Asn Arg Gln Gly Ile Leu Thr Ile Asn Ser Gln Pro Asn Ile Asn>

1480        1490        1500        1510        1520        1530
  x     x     x     x     x     x     x     x     x     x     x     x
GGG AAG CCG TCC TCC GAC CCC ATC GTG GGC TGG GGC CCC AGC GGG GGC TAT
CCC TTC GGC AGG AGG CTG GGG TAG CAC CCG ACC CCG GGG TCG CCC CCG ATA
Gly Lys Pro Ser Ser Asp Pro Ile Val Gly Trp Gly Pro Ser Gly Gly Tyr>

        1540        1550        1560        1570        1580
      x     x     x     x     x     x     x     x     x     x
GTC TTC CAG AAG GCC TAC TTA GAG TTT TTC ACT TCC CGC GAG ACA GCG GAA
CAG AAG GTC TTC CGG ATG AAT CTC AAA AAG TGA AGG GCG CTC TGT CGC CTT
Val Phe Gln Lys Ala Tyr Leu Glu Phe Phe Thr Ser Arg Glu Thr Ala Glu>

      1590        1600        1610        1620        1630
    x     x     x     x     x     x     x     x     x     x
GCA CTT CTG CAA GTG CTG AAG AAG TAC GAG CTC CGG GTT AAT TAC CAC CTT
CGT GAA GAC GTT CAC GAC TTC TTC ATG CTC GAG GCC CAA TTA ATG GTG GAA
Ala Leu Leu Gln Val Leu Lys Lys Tyr Glu Leu Arg Val Asn Tyr His Leu>

      1640        1650        1660        1670        1680
  x     x     x     x     x     x     x     x     x     x
GTC AAT GTG AAG GGT GAA AAC ATC ACC AAT GCC CCT GAA CTG CAG CCG AAT
CAG TTA CAC TTC CCA CTT TTG TAG TGG TTA CGG GGA CTT GAC GTC GGC TTA
Val Asn Val Lys Gly Glu Asn Ile Thr Asn Ala Pro Glu Leu Gln Pro Asn>

      1690        1700        1710        1720        1730
  x     x     x     x     x     x     x     x     x     x
GCT GTC ACT TGG GGC ATC TTC CCT GGG CGA GAG ATC ATC CAG CCC ACC GTA
CGA CAG TGA ACC CCG TAG AAG GGA CCC GCT CTC TAG TAG GTC GGG TGG CAT
Ala Val Thr Trp Gly Ile Phe Pro Gly Arg Glu Ile Ile Gln Pro Thr Val>

    1740        1750        1760        1770        1780
  x     x     x     x     x     x     x     x     x     x     x
GTG GAT CCC GTC AGC TTC ATG TTC TGG AAG GAC GAG GCC TTT GCC CTG TGG
CAC CTA GGG CAG TCG AAG TAC AAG ACC TTC CTG CTC CGG AAA CGG GAC ACC
Val Asp Pro Val Ser Phe Met Phe Trp Lys Asp Glu Ala Phe Ala Leu Trp>
```

Fig. 1E

```
1790        1800        1810        1820        1830
   *     *     *     *     *     *     *     *     *     *
ATT GAG CGG TGG GGA AAG CTG TAT GAG GAG GAG TCC CCG TCC CGC ACC ATC
TAA CTC GCC ACC CCT TTC GAC ATA CTC CTC CTC AGG GGC AGG GCG TGG TAG
Ile Glu Arg Trp Gly Lys Leu Tyr Glu Glu Glu Ser Pro Ser Arg Thr Ile>

1840        1850        1860        1870        1880
   *     *     *     *     *     *     *     *     *     *
ATC CAG TAC ATC CAC GAC AAC TAC TTC CTG GTC AAC CTG GTG GAC AAT GAC
TAG GTC ATG TAG GTG CTG TTG ATG AAG GAC CAG TTG GAC CAC CTG TTA CTG
Ile Gln Tyr Ile His Asp Asn Tyr Phe Leu Val Asn Leu Val Asp Asn Asp>

1890        1900        1910        1920        1930
   *     *     *     *     *     *     *     *     *     *
TTC CCA CTG GAC AAC TGC CTC TGG CAG GTG GTG GAA GAC ACA TTG GAG CTT
AAG GGT GAC CTG TTG ACG GAG ACC GTC CAC CAC CTT CTG TGT AAC CTC GAA
Phe Pro Leu Asp Asn Cys Leu Trp Gln Val Val Glu Asp Thr Leu Glu Leu>

1940        1950        1960        1970        1980        1990
   *     *     *     *     *     *     *     *     *     *     *
CTC AAC AGG CCC ACC CAG AAT GCG AGA GAA ACG GAG GCT CCA TGACCCTGCG
GAG TTG TCC GGG TGG GTC TTA CGC TCT CTT TGC CTC CGA GGT ACTGGGACGC
Leu Asn Arg Pro Thr Gln Asn Ala Arg Glu Thr Glu Ala Pro>

2000        2010        2020        2030        2040        2050
   *     *     *     *     *     *     *     *     *     *     *
TCCTGACGCC CTGCGTTGGA GCCACTCCTG TCCCGCCTTC CTCCTCCACA GTGCTGCTTC
AGGACTGCGG GACGCAACCT CGGTGAGGAC AGGGCGGAAG GAGGAGGTGT CACGACGAAG

2060        2070        2080        2090        2100        2110
   *     *     *     *     *     *     *     *     *     *     *
TCTTGGGAAC TCCACTCTCC TTCGTGTCTC TCCCACCCCG GCCTCCACTC CCCCACCTGA
AGAACCCTTG AGGTGAGAGG AAGCACAGAG AGGGTGGGGC CGGAGGTGAG GGGGTGGACT

2120        2130        2140        2150        2160        2170
   *     *     *     *     *     *     *     *     *     *     *
CAATGGCAGC TAGACTGGAG TGAGGCTTCC AGGCTCTTCC TGGACCTGAG TCGGCCCCAC
GTTACCGTCG ATCTGACCTC ACTCCGAAGG TCCGAGAAGG ACCTGGACTC AGCCGGGGTG

2180        2190        2200        2210        2220
   *     *     *     *     *     *     *     *     *     *
ATGGGAACCT AGTACTCTCT GCTCTAAAAA AAAAAAAAAA AAAGGAATTC
TACCCTTGGA TCATGAGAGA CGAGATTTTT TTTTTTTTTT TTTCCTTAAG
```

Fig. 1F

```
AMVNE ARGNS SLNPC LEGSA SSGSE SSKDS SRCST PGLDP ERHER LREKM RRRLE S--GDKW FSLEF  mthfr
                                          ms ffHas qRdal nqsLa evqGqin vSfEF  ecometf
                                          ms ffHan qREal nqsLa evqGqin vSfEF  stymetf
                                                ms iRdLy haraspf iSLEF  ysRAD1

                                    100.
FPPRT AEGAV NLISR FDRMA AGGPL YIDVT WHPAG DPGSD KETSS MMIAS TAVNY CGLET ILHMT    mthfr
FPPRT sEmeq tLwns iDRls slkPk fvsVT y--ga nsGer drThs i-Ikg ik-dr tGLEa apHlT    ecometf
FPPRT sEmeq tLwns iDRls slkPk fvsVT y--ga nsGer drThs v-Ikg ik-er tGLEa apHlT    stymetf
FPPkT elGtr NLmeR mhRMt AldPL fltVT W--ga -gGtt aEktl t-lAS lAqqt lnipv cmHlT    ysRAD1

                                    *                                 *
CCRQR LEEIT GHLHK AKQLG LKNIM ALRGD -PIGDQ WEEEE GGFNY AVGLV KHIRS EFGDY FDICV   mthfr
Cidat pdElr tiard ywnnG irhIv ALRGD lPpGsg kpE-- ---mY AsdLV tllk- EvaD- FDIsV   ecometf
Cidat rdElr tiard ywnnG irhIv ALRGD lPpGsg kpE-- ---mY AadLV gllk- EvaD- FDIsV   stymetf
Ctnte kaild daLdr cynaG irNIl ALRGn lPIGvv Wlvsq snrll nmrLf)                    ysRAD1
 200.
AGYPK GHPEA GSFEA DLKHL KEKVS AGADF IITQL FFEAD TFFRF VKACT DMGIT CPIVP GIFPI    mthfr
AaYPe vHPEA kSaqA DLlnL KrKVd AGAnr aITQf FFdve sylRF rdrCv saGId veliP GIlPv    ecometf
AaYPe vHPEA kSaqA DLlnL KrKVd AGAnr aITQf FFdve sylRF rdrCv saGId veliP GIlPv    stymetf
                                          300.
QGYHS LRQLV KLSKL EVPQE IKDVI EPIKD NDAAI RN-YGI ELAVS LCQEL LASGL VPGLH FYTLN   mthfr
snfkq akkfa dmtnv riPaw maqmf dgl-D dDAet RklvGa niAmd mvkiL sreG- VkdfH FYTLN   ecometf
snfkq akkfa dmtnv riPsw mslmf Egl-D nDAet RklvGa niAmd mvkiL sreG- VkdfH FYTLN   stymetf

R-EMAT TEVLK RLGMW TEDPR RPLPW ALSAH PKRRE EDVRP IFWAS RPKSY IYRTD EWDEF PNGRW   mthfr
RaEMsy a-ich tLGvr pgl)                                                          ecometf
RaEMsy a-ich tLGvr pgl)                                                          stymetf
      400.
GNSSS PAFGE LKDYY LFYLK SKSPK E  mthfr
```

Fig. 2

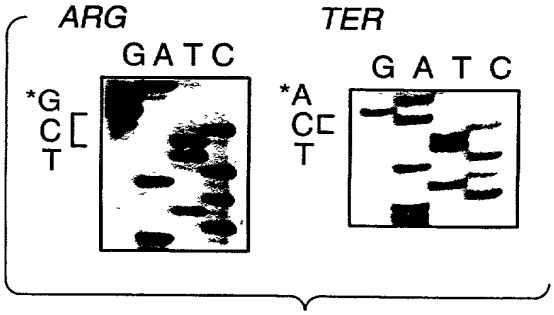

Fig. 3A

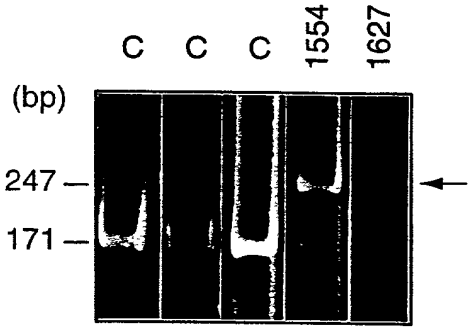

Fig. 3B

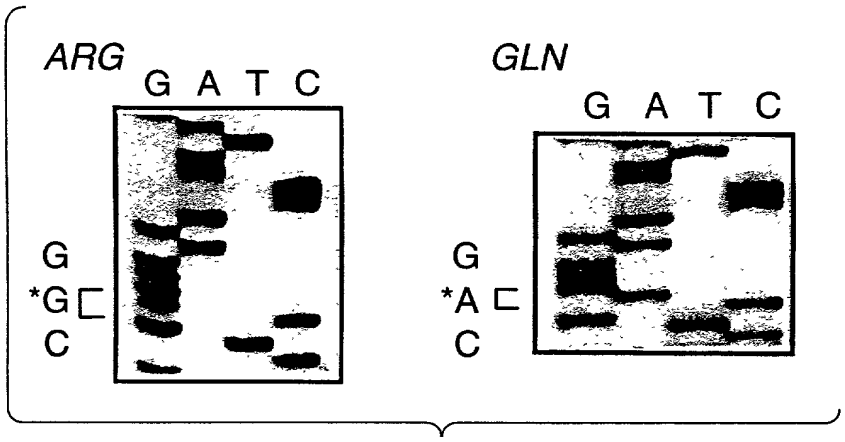

Fig. 4A

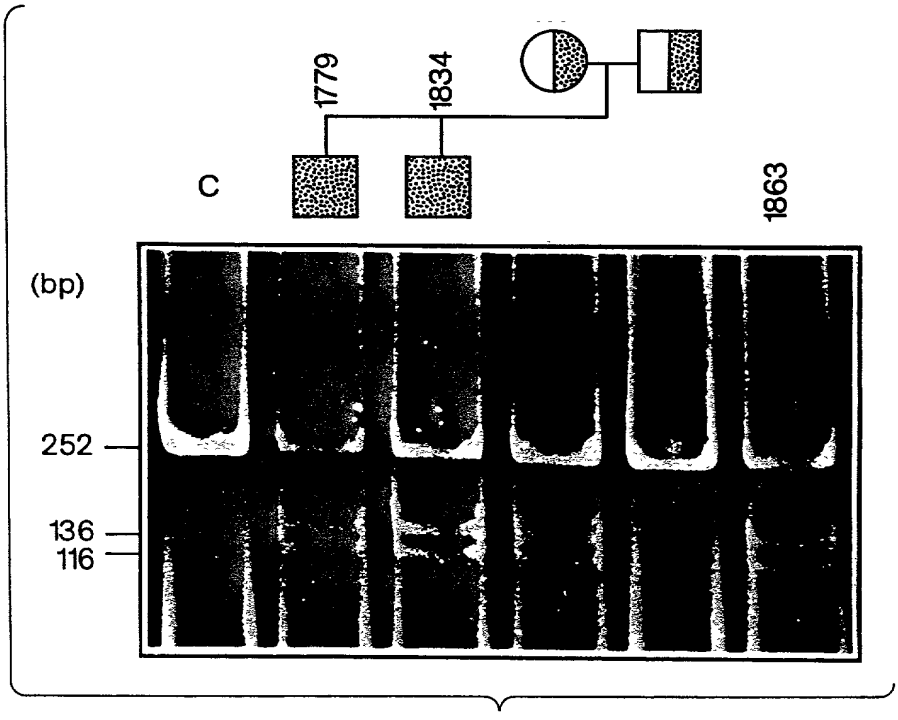

Fig. 4B

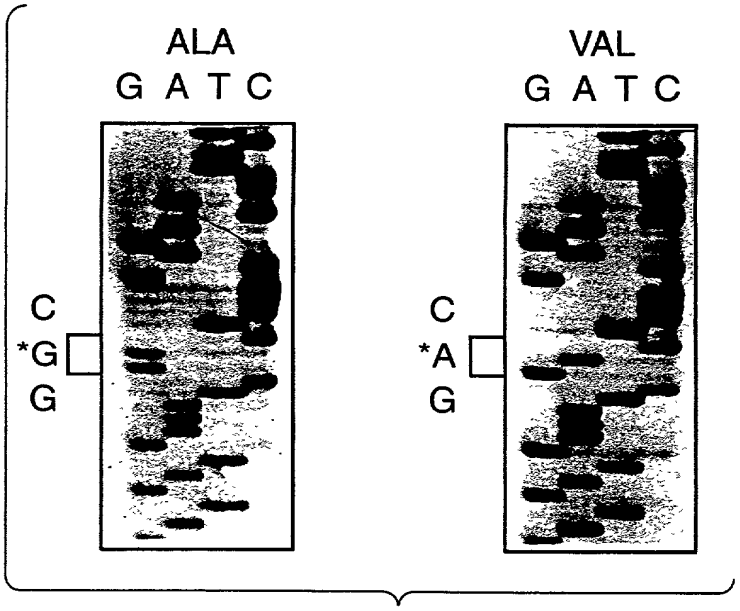

Fig. 5A

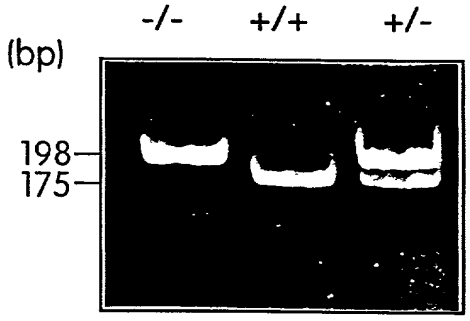

Fig. 5B

```
                 *           *           *           *           *           *
AAT TCC GGA GCC ATG GTG AAC GAA GCC AGA GGA AAC AGC AGC CTC AAC CCC TGC TTG GAG   60
                Met Val Asn Glu Ala Arg Gly Asn Ser Ser Leu Asn Pro Cys Leu Glu   16
                 *           *           *           *           *           *
GGC AGT GCC AGC AGT GGC AGT GAG AGC TCC AAA GAT AGT TCG AGA TGT TCC ACC CCG GGC  120
Gly Ser Ala Ser Ser Gly Ser Glu Ser Ser Lys Asp Ser Ser Arg Cys Ser Thr Pro Gly   36
                 *           *           *           *           *           *
CTG GAC CCT GAG CGG CAT GAG AGA CTC CGG GAG AAG ATG AGG CGG CGA TTG GAA TCT GGT  180
Leu Asp Pro Glu Arg His Glu Arg Leu Arg Glu Lys Met Arg Arg Arg Leu Glu Ser Gly   56
                 *           *           *           *           *           *
GAC AAG TGG TTC TCC CTG GAA TTC TTC CCT CCT CGA ACT GCT GAG GGA GCT GTC AAT CTC  240
Asp Lys Trp Phe Ser Leu Glu Phe Phe Pro Pro Arg Thr Ala Glu Gly Ala Val Asn Leu   76
                 *           *           *           *           *           *
ATC TCA AGG TTT GAC CGG ATG GCA GCA GGT GGC CCC CTC TAC ATA GAC GTG ACC TGG CAC  300
Ile Ser Arg Phe Asp Arg Met Ala Ala Gly Gly Pro Leu Tyr Ile Asp Val Thr Trp His   96
                 *           *           *           *           *           *
CCA GCA GGT GAC CCT GGC TCA GAC AAG GAG ACC TCC TCC ATG ATG ATC GCC AGC ACC GCC  360
Pro Ala Gly Asp Pro Gly Ser Asp Lys Glu Thr Ser Ser Met Met Ile Ala Ser Thr Ala  116
                 *           *           *           *           *           *
GTG AAC TAC TGT GGC CTG GAG ACC ATC CTG CAC ATG ACC TGC TGC CGT CAG CGC CTG GAG  420
Val Asn Tyr Cys Gly Leu Glu Thr Ile Leu His Met Thr Cys Cys Arg Gln Arg Leu Glu  136
                 *           *           *           *           *           *
GAG ATC ACG GGC CAT CTG CAC AAA GCT AAG CAG CTG GGC CTG AAG AAC ATC ATG GCG CTG  480
Glu Ile Thr Gly His Leu His Lys Ala Lys Gln Leu Gly Leu Lys Asn Ile Met Ala Leu  156
                 *           *           *           *           *           *
CGG GGA GAC CCA ATA GGT GAC CAG TGG GAA GAG GAG GAG GGA GGC TTC AAC TAC GCA GTG  540
Arg Gly Asp Pro Ile Gly Asp Gln Trp Glu Glu Glu Glu Gly Gly Phe Asn Tyr Ala Val  176
                 *           *           *           *           *           *
GAC CTG GTG AAG CAC ATC CGA AGT GAG TTT GGT GAC TAC TTT GAC ATC TGT GTG GCA GGT  600
Asp Leu Val Lys His Ile Arg Ser Glu Phe Gly Asp Tyr Phe Asp Ile Cys Val Ala Gly  196
                 *           *           *           *           *           *
TAC CCC AAA GGC CAC CCC GAA GCA GGG AGC TTT GAG GCT GAC CTG AAG CAC TTG AAG GAG  660
Tyr Pro Lys Gly His Pro Glu Ala Gly Ser Phe Glu Ala Asp Leu Lys His Leu Lys Glu  216
                 *           *           *           *           *           *
AAG GTG TCT GCG GGA GCC GAT TTC ATC ATC ACG CAG CTT TTC TTT GAG GCT GAC ACA TTC  720
Lys Val Ser Ala Gly Ala Asp Phe Ile Ile Thr Gln Leu Phe Phe Glu Ala Asp Thr Phe  236
```

Fig. 6A

```
TTC CGC TTT GTG AAG GCA TGC ACC GAC ATG GGC ATC ACT TGC CCC ATC GTC CCC GGG ATC  780
Phe Arg Phe Val Lys Ala Cys Thr Asp Met Gly Ile Thr Cys Pro Ile Val Pro Gly Ile  256

TTT CCC ATC CAG GGC TAC CAC TCC CTT CGG CAG CTT GTG AAG CTG TCC AAG CTG GAG GTG  840
Phe Pro Ile Gln Gly Tyr His Ser Leu Arg Gln Leu Val Lys Leu Ser Lys Leu Glu Val  276

CCA CAG GAG ATC AAG GAC GTG ATT GAG CCA ATC AAA GAC AAC GAT GCT GCC ATC CGC AAC  900
Pro Gln Glu Ile Lys Asp Val Ile Glu Pro Ile Lys Asp Asn Asp Ala Ala Ile Arg Asn  296

TAT GGC ATC GAG CTG GCC GTG AGC CTG TGC CAG GAG CTT CTG GCC AGT GGC TTG GTG CCA  960
Tyr Gly Ile Glu Leu Ala Val Ser Leu Cys Gln Glu Leu Leu Ala Ser Gly Leu Val Pro  316

GGC CTC CAC TTC TAC ACC CTC AAC CGC GAG ATG GCT ACC ACA GAG GTG CTG AAG CGC CTG 1020
Gly Leu His Phe Tyr Thr Leu Asn Arg Glu Met Ala Thr Thr Glu Val Leu Lys Arg Leu  336

GGG ATG TGG ACT GAG GAC CCC AGG CGT CCC CTA CCC TGG GCT CTC AGT GCC CAC CCC AAG 1080
Gly Met Trp Thr Glu Asp Pro Arg Arg Pro Leu Pro Trp Ala Leu Ser Ala His Pro Lys  356

CGC CGA GAG GAA GAT GTA CGT CCC ATC TTC TGG GCC TCC AGA CCA AAG AGT TAC ATC TAC 1140
Arg Arg Glu Glu Asp Val Arg Pro Ile Phe Trp Ala Ser Arg Pro Lys Ser Tyr Ile Tyr  376

CGT ACC CAG GAG TGG GAC GAG TTC CCT AAC GGC CGC TGG GGC AAT TCC TCT TCC CCT GCC 1200
Arg Thr Gln Glu Trp Asp Glu Phe Pro Asn Gly Arg Trp Gly Asn Ser Ser Ser Pro Ala  396

TTT GGG GAG CTG AAG GAC TAC TAC CTC TTC TAC CTG AAG AGC AAG TCC CCC AAG GAG GAG 1260
Phe Gly Glu Leu Lys Asp Tyr Tyr Leu Phe Tyr Leu Lys Ser Lys Ser Pro Lys Glu Glu  416

CTG CTG AAG ATG TGG GGG GAG GAG CTG ACC AGT GAA GCA AGT GTC TTT GAA GTC TTT GTT 1320
Leu Leu Lys Met Trp Gly Glu Glu Leu Thr Ser Glu Ala Ser Val Phe Glu Val Phe Val  436

CTT TAC CTC TCG GGA GAA CCA AAC CGG AAT GGT CAC AAA GTG ACT TGC CTG CCC TGG AAC 1380
Leu Tyr Leu Ser Gly Glu Pro Asn Arg Asn Gly His Lys Val Thr Cys Leu Pro Trp Asn  456

GAT GAG CCC CTG GCG GCT GAG ACC AGC CTG CTG AAG GAG GAG CTG CTG CGG GTG AAC CGC 1440
Asp Glu Pro Leu Ala Ala Glu Thr Ser Leu Leu Lys Glu Glu Leu Leu Arg Val Asn Arg  476
```

Fig. 6B

```
CAG GGC ATC CTC ACC ATC AAC TCA CAG CCC AAC ATC AAC GGG AAG CCG TCC TCC GAC CCC 1500
Gln Gly Ile Leu Thr Ile Asn Ser Gln Pro Asn Ile Asn Gly Lys Pro Ser Ser Asp Pro  496

ATC GTG GGC TGG GGC CCC AGC GGG GGC TAT GTC TTC CAG AAG GCC TAC TTA GAG TTT TTC 1560
Ile Val Gly Trp Gly Pro Ser Gly Gly Tyr Val Phe Gln Lys Ala Tyr Leu Glu Phe Phe  516

ACT TCC CGC GAG ACA GCG GAA GCA CTT CTG CAA GTG CTG AAG AAG TAC GAG CTC CGG GTT 1620
Thr Ser Arg Glu Thr Ala Glu Ala Leu Leu Gln Val Leu Lys Lys Tyr Glu Leu Arg Val  536

AAT TAC CAC CTT GTC AAT GTG AAG GGT GAA AAC ATC ACC AAT GCC CCT GAA CTG CAG CCG 1680
Asn Tyr His Leu Val Asn Val Lys Gly Glu Asn Ile Thr Asn Ala Pro Glu Leu Gln Pro  556

AAT GCT GTC ACT TGG GGC ATC TTC CCT GGG CGA GAG ATC ATC CAG CCC ACC GTA GTG GAT 1740
Asn Ala Val Thr Trp Gly Ile Phe Pro Gly Arg Glu Ile Ile Gln Pro Thr Val Val Asp  576

CCC GTC AGC TTC ATG TTC TGG AAG GAC GAG GCC TTT GCC CTG TGG ATT GAG CGG TGG GGA 1800
Pro Val Ser Phe Met Phe Trp Lys Asp Glu Ala Phe Ala Leu Trp Ile Glu Arg Trp Gly  596

AAG CTG TAT GAG GAG GAG TCC CCG TCC CGC ACC ATC ATC CAG TAC ATC CAC GAC AAC TAC 1860
Lys Leu Tyr Glu Glu Glu Ser Pro Ser Arg Thr Ile Ile Gln Tyr Ile His Asp Asn Tyr  616

TTC CTG GTC AAC CTG GTG GAC AAT GAC TTC CCA CTG GAC AAC TGC CTC TGG CAG GTG GTG 1920
Phe Leu Val Asn Leu Val Asp Asn Asp Phe Pro Leu Asp Asn Cys Leu Trp Gln Val Val  636

GAA GAC ACA TTG GAG CTT CTC AAC AGG CCC ACC CAG AAT GCG AGA GAA ACG GAG GCT CCA 1980
Glu Asp Thr Leu Glu Leu Leu Asn Arg Pro Thr Gln Asn Ala Arg Glu Thr Glu Ala Pro  656

TGA CCC TGC GTC CTG ACG CCC TGC GTT GGA GCC ACT CCT GTC CCG CCT TCC TCC TCC ACA 2040
End

GTG CTG CTT CTC TTG GGA ACT CCA CTC TCC TTC GTG TCT CTC CCA CCC CGG CCT CCA CTC 2100

CCC CAC CTG ACA ATG GCA GCT AGA CTG GAG TGA GGC TTC CAG GCT CTT CCT GGA CCT GAG 2160

TCG GCC CCA CAT GGG AAC CTA GTA CTC TCT GCT CTA AAA AAA AAA AAA AAA AAG GAA TT  2220
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Fig. 6C

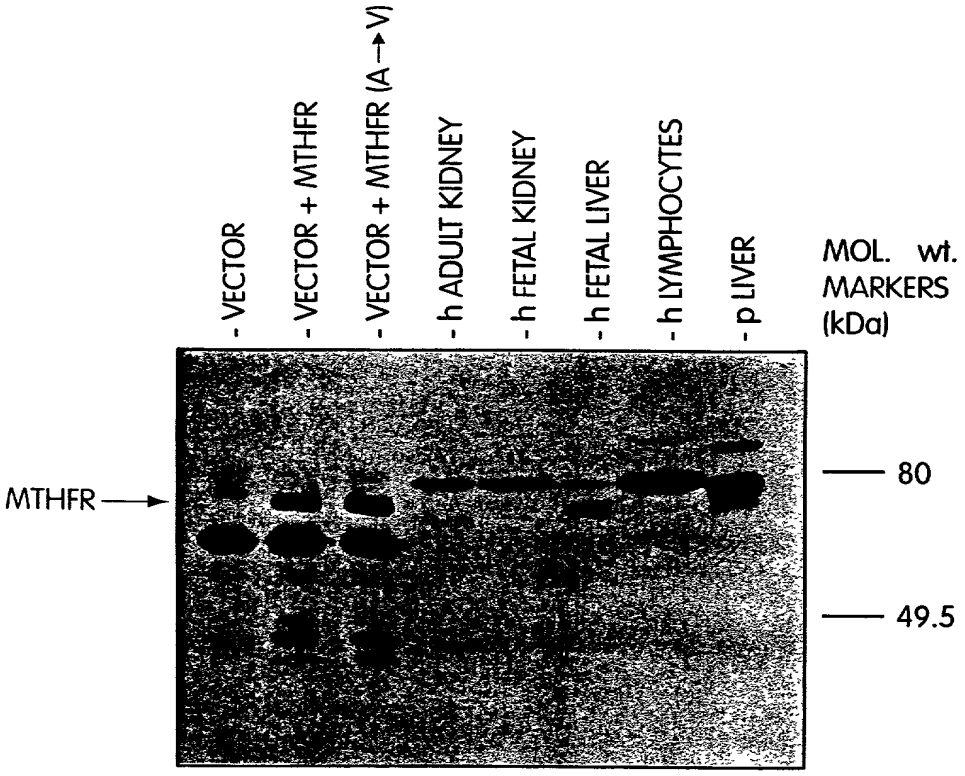

Fig. 7A

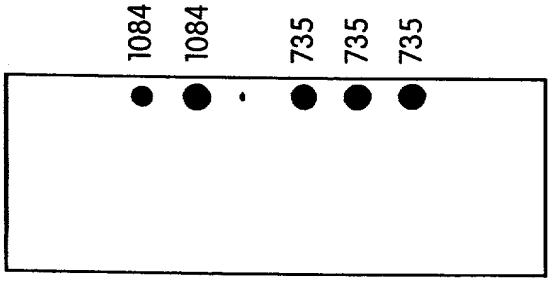

Fig. 10A

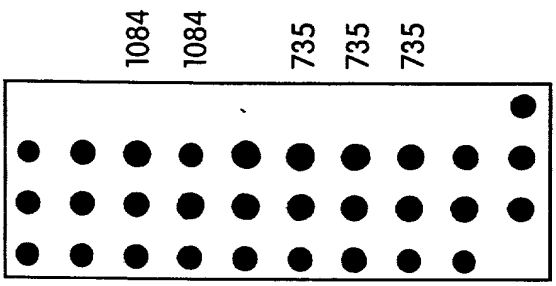

Fig. 10B

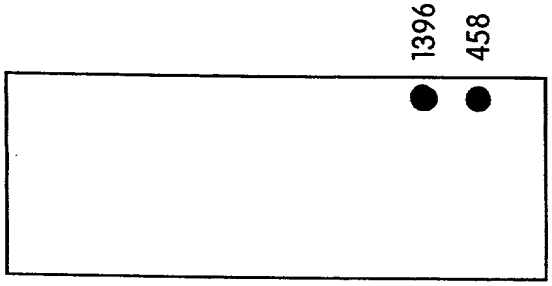

Fig. 10C

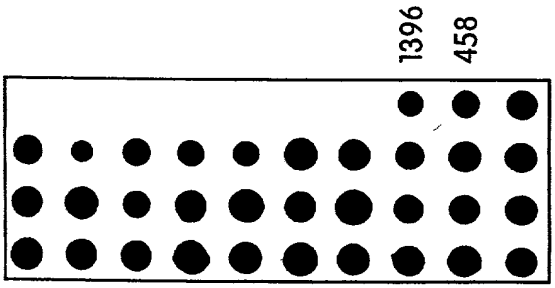

Fig. 10D

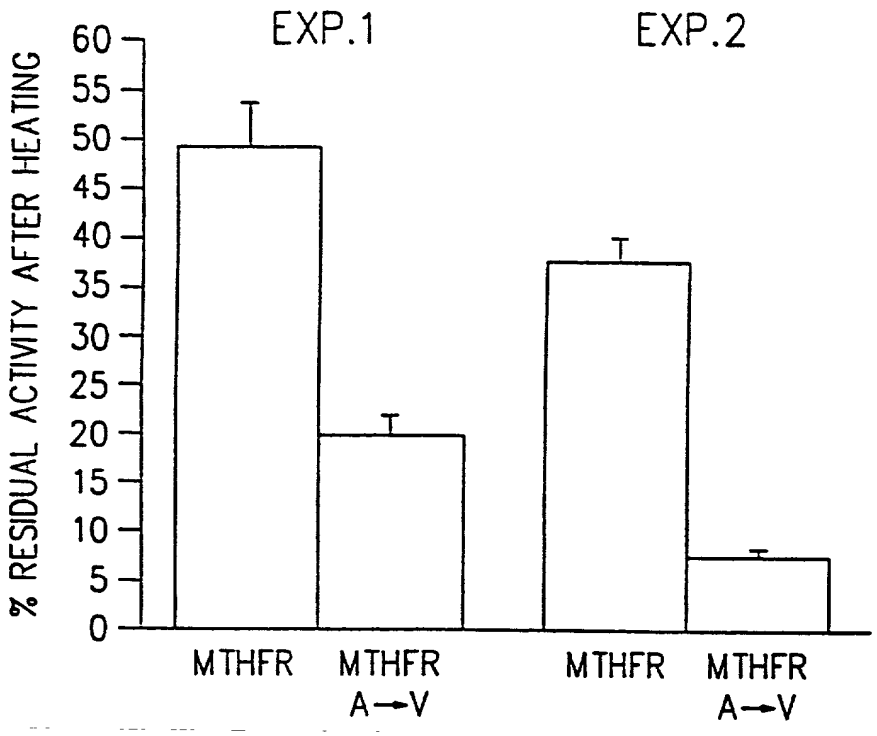

Fig. 7B

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MTHFR:    KHLKEKVSAGADFIITQLFFEADTFFR
            |||  |·      | |  ||·||||
DHFR:     GHLKLFVT----R-IMQD-FESDTFFP
```

Fig. 11

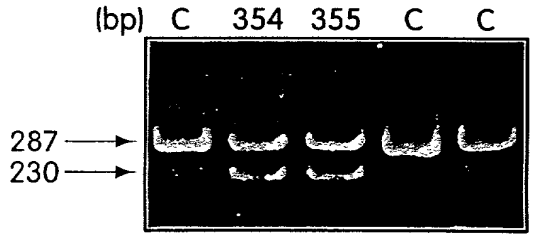
(bp) C 354 355 C C
287
230

Fig. 8A

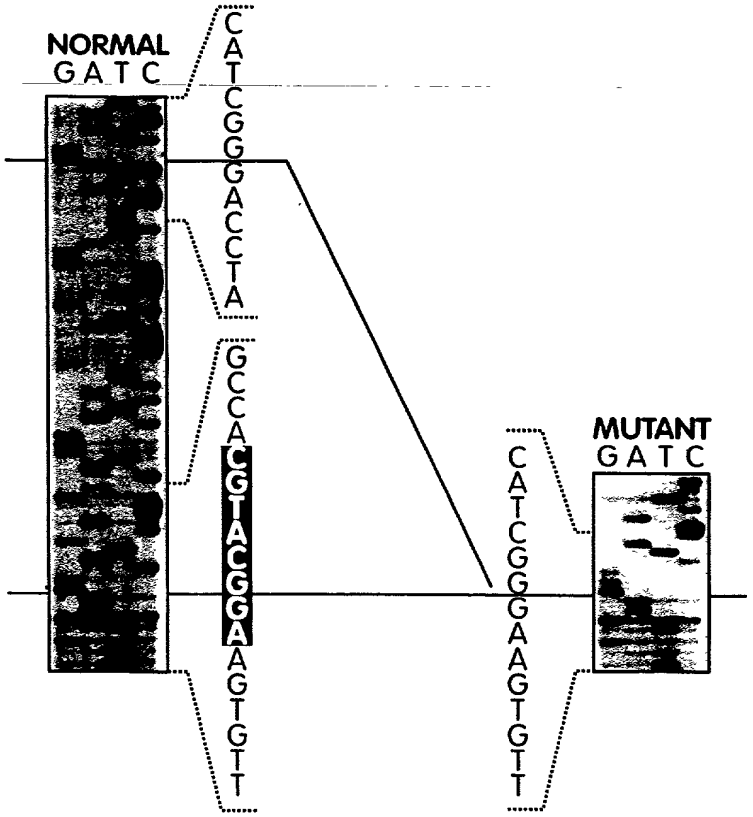
NORMAL
G A T C
C A T C G G G G A C C T A
G C C A C G T A C G G G A A G T G T T
MUTANT
G A T C
C A T C G G G G A A G T G T T

Fig. 8B

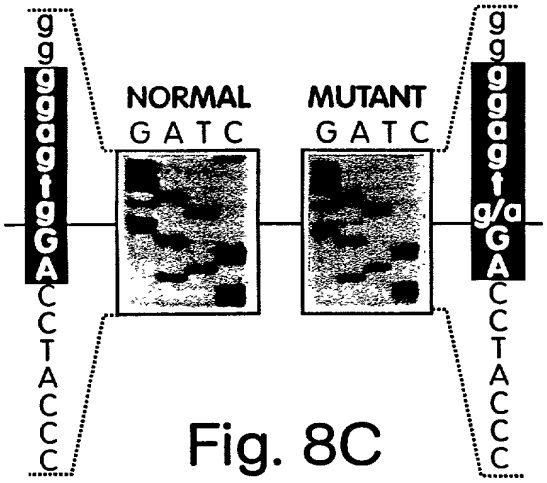
NORMAL
G A T C
MUTANT
G A T C
g g
g g a g t g/a G A
C C T A C C C
g g
g g a g t g A
C C T A C C C

Fig. 8C


(bp)
354
355
C
C
C
175
151

Fig. 8D

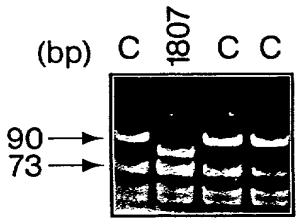

Fig. 9A

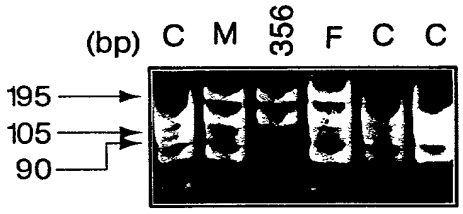

Fig. 9B

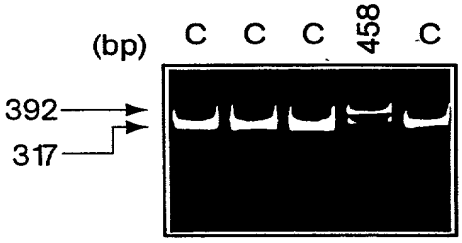

Fig. 9C

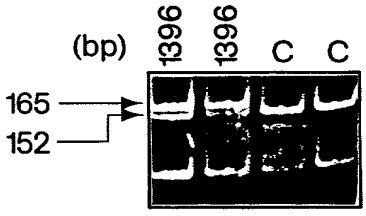

Fig. 9D

EXON 1: 246 bp (bp 3-248)

gggtgtggct gcctgccccc tgatgctccc tgccccaccc tgtgcagtag **GAACCCAGCC**
ATGGTGAACG AAGCCAGAGG AAACAGCAGC CTCAACCCCT GCTTGGAGGG CAGTGCCAGC
AGTGGCAGTG AGAGCTCCAA AGATAGTTCG AGATGTTCCA CCCCGGGCCT GGACCCTGAG
CGGCATGAGA GACTCCGGGA GAAGATGAGG CGGCGATTGG AATCTGGTGA CAAGTGGTTC
TCCCTGGAAT TCTTCCCTCC TCGAACTGCT GAGGGAGCTG TCAATCTCAT CTCAAGgtaa
actcatgcaa ggttaaggtg agaggcggga gtggtggtgc ctgggg

EXON 2: 239 bp (bp 249-487)

acggatgg tatttctcct ggaacctctc ttcagaaaca aacccctacag **GTTTGACCGG**
ATGGCAGCAG GTGGCCCCCT CTACATAGAC GTGACCTGGC ACCCAGCAGG TGACCCTGGC
TCAGACAAGG AGACCTCCTC CATGATGATC GCCAGCACCG CCGTGAACTA CTGTGGCCTG
GAGACCATCC TGCACATGAC CTGCTGCCGT CAGCGCCTGG AGGAGATCAC GGGCCATCTG
CACAAAGCTA AGCAGCTGGG CCTGAAGAAC ATCATGGCGC TGCGGGGAGg tgtggagcca
gcactcccct acactctggg ttctggcttt cccggaggc

EXON 3: 111 bp (bp 488-598)

tctggaggtt gggtgagacc cagtgactat gacctccacc aaccctgcag **ACCCAATAGG**
TGACCAGTGG GAAGAGGAGG AGGGAGGCTT CAACTACGCA GTGGACCTGG TGAAGCACAT
CCGAAGTGAG TTTGGTGACT ACTTTGACAT CTGTGTGGCA Ggtgagtggc tggatcatcc
tggtggcggg gatggagcta gggaggctga

EXON 4: 194 bp (bp 599-792)

ccttgaacag gtggaggcca gcctctcctg actgtcatcc ctattggcag **GTTACCCCAA**
AGGCCACCCC GAAGCAGGGA GCTTTGAGGC TGACCTGAAG CACTTGAAGG AGAAGGTGTC
TGCGGGAGCC GATTTCATCA TCACGCAGCT TTTCTTTGAG GCTGACACAT TCTTCCGCTT
TGTGAAGGCA TGCACCGACA TGGGCATCAC TTGCCCCATC GTCCCCGGGA TCTTTCCCAT
CCAGgtgagg ggcccaggag agcccataag ctccctccac cccactctca ccgc

EXON 5: 251 bp (bp 793-1043)

gctggccagc agccgccaca gcccctcatg tcttggacag **GGCTACCACT CCCTTCGGCA**
GCTTGTGAAG CTGTCCAAGC TGGAGGTGCC ACAGGAGATC AAGGACGTGA TTGAGCCAAT
CAAAGACAAC GATGCTGCCA TCCGCAACTA TGGCATCGAG CTGGCCGTGA GCCTGTGCCA
GGAGCTTCTG GCCAGTGGCT TGGTGCCAGG CCTCCACTTC TACACCCTCA ACCGCGAGAT
GGCTACCACA GAGGTGCTGA AGCGCCTGGG GATGTGGACT GAGGACCCCA Ggtgagggca
gtggcccaga gatccccaga ggagggtcca agagcagccc c

EXON 6: 135 bp (bp 1044-1178)

tccctctagc caatcccttg tctcaattct ctgtccccat cctcacccag **GCGTCCCCTA**
CCCTGGGCTC TCAGTGCCCA CCCCAAGCGC CGAGAGGAAG ATGTACGTCC CATCTTCTGG
GCCTCCAGAC CAAAGAGTTA CATCTACCGT ACCCAGGAGT GGGACGAGTT CCCTAACGGC
CGCTGgtgag ggcctgcaga ccttccttgc aaatacatct ttgttcttgg gagcg

Fig. 12A

EXON 7: 181 bp (bp 1179-1359)

actgccctct gtcaggagtg tgccctgacc tctgggcacc cctctgccag **GGGCAATTCC**
TCTTCCCCTG CCTTTGGGGA GCTGAAGGAC TACTACCTCT TCTACCTGAA GAGCAAGTCC
CCCAAGGAGG AGCTGCTGAA GATGTGGGGG GAGGAGCTGA CCAGTGAAGC AAGTGTCTTT
GAAGTCTTTG TTCTTTACCT CTCGGGAGAA CCAAACCGGA ATGGTCACAA Agtgagtgat
gctggaagtg gggaccctgg ttcatcccct gcccctggcc t

EXON 8: 183 bp (bp 1360-1542)

cagggtgcca aacctgatgg tcgccccagc cagctcaccg tctctcccag **GTGACTTGCC**
TGCCCTGGAA CGATGAGCCC CTGGCGGCTG AGACCAGCCT GCTGAAGGAG GAGCTGCTGC
GGGTGAACCG CCAGGGCATC CTCACCATCA ACTCACAGCC CAACATCAAC GGGAAGCCGT
CCTCCGACCC CATCGTGGGC TGGGGCCCCA GCGGGGGCTA TGTCTTCCAG AAGgtgtggt
agggaggcac ggggtgcccc cctctcttga ccggcacccg tgg

EXON 9: 102 bp (bp 1543-1644)

gggcgtctgg cagggctggg gttggtgaca ggcacctgtc tctcccacag **GCCTACTTAG**
AGTTTTTCAC TTCCCGCGAG ACAGCGGAAG CACTTCTGCA AGTGCTGAAG AAGTACGAGC
TCCGGGTTAA TTACCACCTT GTCAATGTGA AGgtaggcca ggccccacgg ttcccacaga
gtaccaggcc cttcgttgaa ca

EXON 10: 120 bp (bp 1645-1764)

actccagttg ttcttggccc aggtcttacc cccaccccac atcccctcag **GGTGAAAACA**
TCACCAATGC CCCTGAACTG CAGCCGAATG CTGTCACTTG GGGCATCTTC CCTGGGCGAG
AGATCATCCA GCCCACCGTA GTGGATCCCG TCAGCTTCAT GTTCTGGAAG gtaaaggagc
gggggcaagc ttgccccgcc cacctggaaa accgtgggga

EXON 11: 219 bp (stop codon) (bp 1765-1983)
432 bp (end of cDNA) (bp 1765-2196)

ctctgtgtgt gtgtgcatgt gtgcgtgtgt gcgggggtat gtgtgtgtag **GACGAGGCCT**
TTGCCCTGTG GATTGAGCGG TGGGGAAAGC TGTATGAGGA GGAGTCCCCG TCCCGCACCA
TCATCCAGTA CATCCACGAC AACTACTTCC TGGTCAACCT GGTGGACAAT GACTTCCCAC
TGGACAACTG CCTCTGGCAG GTGGTGGAAG ACACATTGGA GCTTCTCAAC AGGCCCACCC
AGAATGCGAG AGAAACGGAG GCTCCATGAC CCTGCGTCCT GACGCCCTGC GTTGGAGCCA
CTCCTGTCCC GCCTTCCTCC TCCACAGTGC TGCTTCTCTT GGGAACTCCA CTCTCCTTCG
TGTCTCTCCC ACCCCGGCCT CCACTCCCCC ACCTGACAAT GGCAGCTAGA CTGGAGTGAG
GCTTCCAGGC TCTTCCTGGA CCTGAGTCGG CCCCACATGG GAACCTAGTA CTCTCTGCTC
TAgccaggag tctgtgctct tttggtgggg agcacttgct cctgcagagg ac

Fig.12B

EXON 1: 243 bp (bp 3-245)

gggtttggta ccagccctat aataccccg gcccccaccc tctacagcag **GAATCCAGCC**
ATGGTGAACG AGGCCAGAGG AAGTGGCAGT CCCAACCCGC GATCTGAGGG CAGCAGCAGT
GGCAGCGAGA GTTCCAAGGA CAGTTCAAGA TGTTCCACCC CCAGCCTGGA CCCAGAGCGG
CACGAGAGAC TCCGGGAGAA GATGAGGCGC AGAATGGACT CTGGTGACAA GTGGTTCTCC
CTGGAGTTCT TCCCCCCTCG AACTGCTGAG GGAGCTGTTA ACCTCATCTC CAGgtgagta
gggaggttaa tccgcggggg tcggcaggct tcaggggagc gtg

EXON 2: 239 bp (bp 246-484)

gagctcccta tttaccccag gagcctactt aaggaggaaa tcccctacag **GTTTGACCGG**
ATGGCAGCAG GGGGCCCCCT CTTCGTAGAT GTTACCTGGC ACCCAGCTGG AGACCCTGGC
TCAGACAAGG AGACCTCCTC CATGATGATC GCCAGCACAG CAGTAAACTA CTGCGGCTTG
GAAACCATCC TGCATATGAC CTGCTGCCAG CAGCGCCCGG AGGAGATCAC AGGCCATCTG
CACAGAGCCA AGCAGCTGGG CCTGAAGAAC ATAATGGCGC TGAGGGGAGg tgtggcgcca
gcacccctcc tctttgggtt cttgctttcc tgaaggctt

EXON 3: 111 bp (bp 485-595)

tctggaggtc aggggacacc cagtgaccat gacctccagc aaccctgcag **ACCCTGTAGG**
TGACCACTGG GAAGCAGAGG AAGGAGGCTT CAGCTATGCC ACAGACCTGG TGAAGCACAT
CCGGACCGAG TTTGCTGACT ATTTTGACAT CTGTGTGGCA Ggtaagtgag gacagagaag
ggtcaggatg agaggatagc cagctagtct t

EXON 4: 194 bp (bp 596-789)

gcaggtaggt tgagaccagc cccctactc ttcttgtctc ctcctggtag **GTTACCCCAG**
AGGCCACCCC GATGCAGAGA GCTTCGAGGA TGACCTGAAG CATTTGAAGG AGAAGGTATC
TGCAGGCGCC GACTTCATTA TCACTCAGCT CTTCTTTGAG GCCAGCACCT TCTTCAGCTT
TGTGAAGGCC TGCACAGAGA TAGGCATCTC TTGCCCTATC CTGCCTGGGA TCTTCCCTAT
TCAGgtgagg ggcttgggag gacctgattc cctccgtcca gtgcatgcgg aagt

EXON 5: 251 bp (bp 790-1040)

cagtggagca taggccagag atgaccccat gcccttgtg tctctgacag **GGCTACACTT**
CCCTTCGGCA GCTTGTAAAA CTGTCCAAGC TGGAGGTGCC ACAGAAGATC AAGGATGTAA
TTGAGCCCAT CAAAGACAAC GATGCTGCCA TCCGCAACTA CGGCATTGAG CTGGCTGTAA
GGCTGTGCCG GGAGCTGCTG GACAGTGGCT TGGTGCCAGG CCTCCACTTC TATACCCTCA
ACCGCGAGGT GGCCACCATG GAGGTGCTAA AGCAACTGGG CATGTGGACC GAGGACCCCA
Ggtgagcggt ggaagctgga ggcataccca tgagtcagag tcgcgcaggt g

EXON 6: 135 bp (bp 1041-1175)

ctagctcagt ctacctaagc ccttgtcttt tccctcttcc ttccctccag **GCGTCCCTTG**
CCCTGGGCTC TCAGTGCGCA TCCCAAGCGC CGGGAGGAAG ATGTCCGTCC CATCTTCTGG
GCCTCCAGAC CAAAGAGCTA CATCTACCGC ACACAGGACT GGGATGAGTT TCCTAACGGC
CGCTGgtgag gagagaagcc agggggtgtt aggaattgct ggtgcctggg tggaa

Fig. 13A

EXON 7: 181 bp (bp 1176-1356)

aataggacaa gatttacaac aaagtgcctt gtcccttata ctcctgccag **GGGTAATTCT**
TCCTCACCAG CCTTTGGGGA GCTGAAAGAC TACTACCTCT TCTACCTGAA AAGCAAGTCC
CCCAGGGAGG AGCTGCTGAA GATGTGGGGC GAGGAGCTCA CCAGCGAAGA GAGTGTCTTT
GAAGTCTTTG AACACTACCT CTCTGGAGAG CCGAATCGCC ATGGCTACAG Agtgagtggg
gtgaggagga acggcccagc tttgtctcag ccttgg

EXON 8: 183 bp (bp 1357-1539)

cccagtccca gactcagtgc tgccctcgct cagcgcaccc tgccctgcag **GTAACCTGCC**
TGCCCTGGAA CGATGAACCC CTGGCAGCGG AAACCAGCCT GATGAAGGAA GAGCTGCTCC
GCGTGAACAG GCTGGGCATC CTCACCATCA ACTCTCAGCC CAACATCAAC GCAAAACCAT
CCTCAGACCC TGTTGTGGGC TGGGGCCCCA GTGGGGGTTA TGTCTTCCAG AAGgtatgct
aggatgcagt actctcgata tccccaggga ctgacacaga acc

EXON 9: 102 bp (bp 1540-1641)

gagaacttgg caagtagtgg ggttgacatg ttgggtgtat tctccctcag **GCCTACCTCG**
AATTCTTCAC CTCCCGTGAA ACTGTGGAGG CGCTTCTGCA GGTGCTGAAG ACATACGAGC
TGCGGGTCAA CTACCACATC GTGGACGTGA AGgtaagcca gctccctccg gcttagacgc
agcaaggctt gaaaacacct aca

EXON 10: 120 bp (bp 1642-1761)

agcagtggga ggttgcggtc accctgcctc agccctgcct ctgttctcag **GGAGAGAACA**
TCACTAATGC CCCTGAGCTG CAGCCCAATG CCGTGACGTG GGGCATCTTC CCGGGTCGAG
AGATCATCCA GCCTACTGTG GTGGACCCCA TCAGCTTCAT GTTCTGGAAG gtaagggagt
gggagggagt ggaggaccct ggctaccgtg agagcccag

EXON 11: 216 bp (stop codon) (bp 1762-1977)

ggaggtacca gccgtgctga ccctgctcgt gtgtctctgt tcacacgtag **GATGAGGCCT**
TTGCCCTGTG GATCGAGCAG TGGGGCAAGC TATACGAGGA GGAGTCGCCA TCCCGCATGA
TCATCCAATA CATCCATGAC AACTATTTCC TGGTCAACCT GGTGGACAAC GAGTTCCCGC
TGGACAGCTG CCTGTGGCAG GTGGTGGAGG ACACGTTTGA GCTGCTCAAC AGGCATCCCA
CGGAGAGAGA GACACAGGCT CCATGAgcct gcatctctca acaggcacac catggagaga
gagacacagg ctctgtgagc cgtgcatccc tcaacaggca caccacggag agagagacac
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ctacaca

Fig. 13B

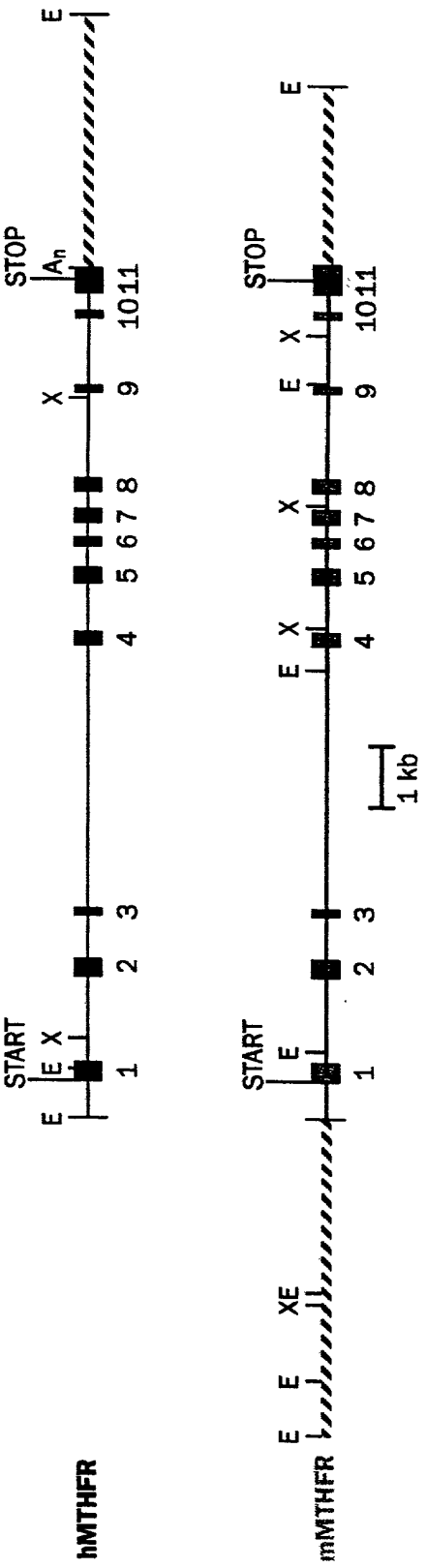
hMTHFR
START
E X
E
1 2 3 4 5 6 7 8 X 9 10 11
STOP
A_n
E
mMTHFR
E E XE
START
E
E X
1 2 3 4 5 6 7 8 X 9 10 11
STOP
E X
E
1 kb

Fig. 14

```
hMTHFR MVNEARGNSSLNPCLEGSASSGSESSKDSSRCSTPGLDPERHERLREKMRRRLESGDKWF
mMTHFR ▯▯▯▯▯▯▯sg▯ps▯rs▯▯▯-▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯s▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯mds▯▯▯▯▯
bMTHFR ----------------------------------fhasqrda▯nqsl-aevq-▯qinv

hMTHFR SLEFFPPRTAEGAVNLISRFDRMAAGGPLYIDVTWHPAGDPGSDKETSSMMIASTAVNYC
mMTHFR ▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯fv▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯
bMTHFR ▯f▯▯▯▯▯▯▯s▯meqt▯wnsi▯▯lssslk▯kfvs▯▯-yg▯-ns▯erdr▯h▯--▯kgik-drt

hMTHFR GLETILHMTCCRQRLEEITGHLHKAKQLGLKNIMALRGDPIGDQWEEEEGGFNYAVDLVK
mMTHFR ▯▯▯▯▯▯d▯▯▯▯▯q▯▯p▯▯▯▯▯▯▯▯r▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯v▯▯h▯▯a▯▯▯▯▯s▯▯t▯▯▯▯
bMTHFR ▯▯▯aap▯l▯▯idatpd▯lrtiardywnn▯irh▯v▯▯▯▯▯lpp-gsgkp▯m---▯▯s▯▯▯t

hMTHFR HIRSEFGDYFDICVAGYPKGHPEAGSFEADLKHLKEKVSAGADFIITQLFFEADTFFRFV
mMTHFR ▯▯▯t▯▯a▯▯▯▯▯▯▯▯▯▯▯r▯▯▯d▯e▯▯▯d▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯s▯▯▯s▯▯
bMTHFR 11k-▯va▯-▯▯▯s▯▯a▯▯ev▯▯▯▯k▯aq▯▯▯ln▯▯r▯▯d▯▯▯nra▯▯▯f▯▯dvesyl▯▯r

hMTHFR KACTDMGITCPIVPGIFPIQGYHSLRQLVKLSKLEVPQEIKDVIEPIKDNDAAIRNYGIE
mMTHFR ▯▯▯▯ei▯▯s▯▯▯l▯▯▯▯▯▯▯▯▯t▯▯▯▯▯▯▯▯▯▯▯▯▯k▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯
bMTHFR dr▯vsa▯▯dve▯i▯▯▯l▯vsnfkqakkfadmtnvri▯awmaqmfdgldDdaetrklv▯an

hMTHFR LAVSLCQELLASGLVPGLHFYTLNREMATTEVLKRLGMWTEDPRRPLPWALSAHPKRREE
mMTHFR ▯▯▯x▯▯r▯▯▯dS▯▯▯▯▯▯▯▯▯▯▯▯▯v▯▯m▯▯▯▯q▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯
bMTHFR i▯mdmvk-i▯sreg▯kdf▯▯▯▯▯▯▯aemsyaicht▯▯vr----------

hMTHFR DVRPIFWASRPKSYIYRTQEWDEFPNGRWGNSSSPAFGELKDYYLFYLKSKSPKEELLKM
mMTHFR ▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯d▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯r▯▯▯▯▯▯
bMTHFR ------------------------------------------------------------

hMTHFR WGEELTSEASVFEVFVLYLSGEPNRNGHKVTCLPWNDEPLAAETSLLKEELLRVNRQGIL
mMTHFR ▯▯▯▯▯▯▯▯e▯▯▯▯▯▯eh▯▯▯▯▯▯▯▯h▯yr▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯m▯▯▯▯▯▯▯▯l▯▯▯
bMTHFR ------------------------------------------------------------

hMTHFR TINSQPNINGKPSSDPIVGWGPSGGYVFQKAYLEFFTSRETAEALLQVLKKYELRVNYHL
mMTHFR ▯▯▯▯▯▯▯▯▯a▯▯▯▯▯▯v▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯v▯▯▯▯▯▯▯t▯▯▯▯▯▯▯i
bMTHFR ------------------------------------------------------------

hMTHFR VNVKGENITNAPELQPNAVTWGIFPGREIIQPTVVDPVSFMFWKDEAFALWIERWGKLYE
mMTHFR ▯d▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯i▯▯▯▯▯▯▯▯▯▯▯▯▯q▯▯▯▯▯▯
bMTHFR ------------------------------------------------------------

hMTHFR EESPSRTIIQYIHDNYFLVNLVDNDFPLDNCLWQVVEDTLELLNRPTQNARETEAP
mMTHFR ▯▯▯▯▯▯m▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯▯e▯▯▯▯s▯▯▯▯▯▯▯▯▯f▯▯▯▯▯h-pte▯▯▯q▯▯
bMTHFR ------------------------------------------------------------
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Fig. 15